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Intensive Care Mortality Prognostic Model for Pediatric Pulmonary Hypertension

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Abstract

Objective—The disease burden and mortality of children with pulmonary hypertension (PH) are significantly higher than for the general pediatric intensive care unit (PICU) population. We aimed to develop a risk-adjustment tool predicting PICU mortality for pediatric PH patients: the Pediatric Index of Pulmonary Hypertension Intensive Care Mortality (PIPHM) score.

Design—Retrospective analysis of prospectively collected multicenter pediatric critical care data.

Setting—143 centers submitting data to Virtual Pediatric Systems database between January 1, 2009 and December 31, 2015.

Patients—Patients 21 years or younger with a diagnosis of PH.

Interventions—Twenty-one demographic, diagnostic, and physiologic variables obtained within 12 hours of PICU admission were assessed for inclusion. Multivariable logistic regression with stepwise selection was performed to develop the final model. Receiver operating characteristic (ROC) curves were used to compare the PIPHM score to Pediatric Risk of Mortality-3 (PRISM-3) and Pediatric Index of Mortality-2 (PIM-2) scores.

Measurements and Main Results—14,268 admissions with a diagnosis of PH were included. Primary outcome was PICU mortality. Fourteen variables were selected for the final model: age, bradycardia, systolic hypotension, tachypnea, pH, FiO₂, hemoglobin, blood urea nitrogen,

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creatinine, mechanical ventilation, non-elective admission, previous PICU admission, PICU admission due to non-surgical cardiovascular disease, cardiac arrest immediately prior to admission. The ROC curve for the PIPHM model (area under the curve (AUC) = 0.77) performed significantly better than the ROC curves for PRISM-3 (AUC = 0.71, $p < 0.001$) and PIM-2 (AUC = 0.69, $p < 0.001$), respectively.

Conclusions—The PIPHM score is a parsimonious model that performs better than PRISM-3 and PIM-2 for mortality in a multicenter cohort of pediatric PH patients admitted to PICUs. Application of the PIPHM model to PH patients in the PICU might facilitate earlier identification of patients at high risk for mortality and improve the ability to prognosticate for patients and families.

Keywords

pulmonary hypertension; pulmonary vascular disease; pediatric pulmonary hypertension; pediatric critical care illness severity scores; Pediatric Index of Mortality-2; Pediatric Risk of Mortality-3

Introduction

Pulmonary hypertension (PH) in children, defined as elevated resting mean pulmonary artery pressure (mPAP > 25 mmHg), may be primary (idiopathic or genetic) or secondary to a variety of underlying etiologies, including cardiovascular, respiratory, and systemic conditions (1). Knowledge about outcomes and hospital course of patients with PH admitted to the pediatric intensive care unit (PICU) is relatively scarce. We have previously shown that the disease burden and mortality of children with PH are significantly higher than for the general PICU population (2). Compared to children in the PICU without PH, those with PH have a higher mortality rate (6.8% vs. 2.3%), longer length of stay, and are more likely to require invasive interventions, including mechanical ventilation and cardiopulmonary resuscitation (2). Children with PH were also found to have higher pediatric critical care illness severity scores, including Pediatric Index of Mortality-2 (PIM-2) (3, 4) and Pediatric Risk of Mortality-3 (PRISM-3), compared to their peers without PH (5, 6). However, the individual components that comprise these scores were not assessed in this prior study.

Illness severity scoring systems provide a standardized assessment of predicted mortality based upon physiologic and clinical data collected around the time of admission to the PICU (7, 8). Risk adjustment tools can be useful in identification of patients at highest risk for mortality in both clinical practice and research. However, these tools were developed from heterogeneous patient populations and may be less applicable to subpopulations of patients within the PICU (7, 9–13). To that end, a variety of pediatric diagnosis-specific prognostic models have been developed, including those relevant to multiple organ dysfunction syndrome (14, 15), acute respiratory distress syndrome (16), oncology (17), liver failure (18), cardiac intensive care (19), cardiac surgery (20, 21), and extracorporeal membrane oxygenation (ECMO) (22, 23).

Given the life-threatening nature of PH and high risk for cardiorespiratory collapse without swift and appropriate treatment, early identification of PH patients at particularly high risk for mortality may improve outcomes (24). To date, no risk-adjustment tool exists for

critically ill children or adults with PH. Therefore, we aimed to develop a new risk-adjustment tool predicting mortality for pediatric PH patients in the PICU: the Pediatric Index of Pulmonary Hypertension Intensive Care Mortality (PIPHM) score.

Materials & Methods

Study Design

This is a post-hoc analysis of multicenter data from the Virtual Pediatric Systems (VPS), LLC database. VPS is a comprehensive PICU database that prospectively tracks information about demographics, diagnoses, procedures, outcomes, and illness severity scores. The database includes 153 PICUs, most of which are located in the United States. Institutional review board approval by the University of California San Francisco was obtained. Epidemiology and baseline characteristics of patients with primary and secondary PH in the VPS database have previously been described by our group (2).

Data Collection

The study population included all PICU admissions between January 1, 2009 and December 31, 2015 recorded in the VPS database. VPS diagnosis codes and *International Classification of Diseases, Ninth Revision (ICD9)* codes (ICD9 416 or ICD9 416.8) were queried to identify admissions associated with a diagnosis of PH. Newborns with exclusive diagnoses of persistent pulmonary hypertension of the newborn (PPHN) or those with both a diagnosis of PPHN and secondary PH under 30 days of age at time of admission were excluded from this analysis. To ensure the completeness and availability of physiologic data for this study, only centers collecting and reporting data for calculation of PIM-2 and PRISM-3 were included (n=143). Those admissions with PRISM-3 scores missing were excluded from the final training and validation dataset so that the same validation dataset could be used for the PRISM-3 score.

Variables

A total of 21 demographic (age, gender), diagnostic (prematurity, PH group), and physiologic candidate variables were assessed for inclusion in the model (Table 1). Age at admission was stratified into six categories based upon those used in the Pulmonary Vascular Research Institute Functional Classification of Pulmonary Hypertension in Children ("Pediatric Functional Class") guidelines (0-6 months, >6 to 12 months, >12 months to 2 years, > 2 to 5 years, > 5 to 16 years, and > 16 years) (25). Physiologic variables included those collected prospectively by each center to calculate PIM-2 and PRISM-3 within the first hour and first 12 hours of PICU admission, respectively. Only variables that are relevant to severity of PH based upon physiology were assessed as candidate variables. Normal vital sign ranges for age were defined based upon consensus guidelines and clinical judgment (26–28). The majority of variables were dichotomized and none of the variables were left as continuous in an effort to allow the model to be more readily converted into a simple bedside tool in the future. Specific rationales for handling of each variable are provided (footnotes in Table 2). Consistent with standard reporting and calculation of PIM-2 (3, 4) and PRISM-3 (5, 6) scores, in which the assumption is made that missing data are not abnormal enough to merit points towards the score, the value of each variable was

considered to be in the normal range if not reported in the dataset (e.g. pH assumed to be >7.3 if no value entered).

Statistics

The data were divided randomly into a training dataset (n=10,472, 75% of cohort) and validation dataset (n=3,490, 25% of cohort). The following steps were performed to develop the model: 1) Univariate logistic analyses were performed on the entire dataset to analyze the association of each candidate variable on PICU mortality. Non-independence for multiple admissions of the same patients was accounted for by clustering by unique patient identifier code; 2) Variables with p values <0.05 in univariate analyses were considered for inclusion in the multivariable logistic model; 3) Stepwise backward selection was performed in the training dataset by dropping variables with p-values > 0.05 one at a time until all variables showed a p-value < 0.05. The model was then applied to the validation dataset to rule out overfitting.

Results were presented in odds ratios (OR) and 95% confidence intervals (CI). $P < 0.05$ was considered statistically significant. Receiver operating characteristic (ROC) curves were used to compare the PIPHM score to PRISM-3 and PIM-2 scores. Data analysis was performed using Stata (version 13, StataCorp, College Station, Texas, USA).

Results

From the original cohort of 14,880 admissions with PH identified from 670,098 admissions in the VPS database (2.2%) (2), 612 were excluded because those admissions were associated with units that did not collect PRISM-3 data (n=14,268). An additional 306 admissions were excluded from the multivariable analyses because PRISM-3 scores were missing (n=13,962), likely because these cases met exclusion criteria for the calculation of PRISM-3 as defined in the PRISM-3 derivation (5, 6). Median age at admission was 16.4 months (interquartile range 6.2 months – 4.2 years), 49% were male, 16% had a history of prematurity, and 86% had a diagnosis of secondary PH. Overall mortality rate was 6.8% (971/14,268); mortality rate was significantly higher for those with primary PH (8.4 vs. 6.5%, $p=0.003$).

In univariate analysis of the entire dataset, 18 of the 21 candidate variables were found to be significantly associated with mortality (Table 2): age, PH group, FiO₂, mechanical ventilation, systolic blood pressure, heart rate, respiratory rate, pH, base deficit, arterial partial pressure of oxygen (PaO₂), arterial partial pressure of carbon dioxide (PaCO₂), hemoglobin, blood urea nitrogen (BUN), creatinine, non-elective admission, previous PICU admission, PICU admission due to non-surgical cardiovascular disease, and cardiac arrest immediately prior to admission. Given collinearity with pH, base deficit was excluded. The decision was made to exclude PaO₂ because this could not be adjusted for FiO₂ as these variables may not have been collected from the same point in time. Of the 16 variables entered in the multivariable analysis, PH group (primary versus secondary) and PaCO₂ were excluded for p values > 0.05. A total of 14 variables remained in the final model (Table 3).

The results from multivariable analyses are shown in Table 4. Factors associated with the greatest odds of mortality in multivariable analysis included mechanical ventilation (OR 2.1; 95% CI 1.7-2.6), hemoglobin <6 mg/dl (OR 2.5; 95% CI 1.1-5.7), non-elective PICU admission (OR 2.9; 95% CI 2.3-3.7), and cardiac arrest immediately prior to admission (OR 2.6; 95% CI 1.9-3.5) (Table 4). ROC curves were generated from application of the PIPHM model to the training and validation datasets (area under the curve (AUC) = 0.80 and 0.77, respectively) and were compared to those for PRISM-3 (AUC = 0.75 and AUC = 0.71, $p < 0.001$ for both comparisons) and PIM-2 (AUC = 0.72 and AUC = 0.69, $p < 0.001$ for both comparisons) (Figures 1 and 2).

Discussion

There are no risk-adjustment tools for mortality in pediatric PH. This study is the first to provide a prognostic tool for identification of children at greatest risk for mortality in the PICU setting. The PIPHM model was developed within a large multicenter cohort of PICU admissions with PH diagnoses over a 7-year period and validated in a separate subset of this cohort.

Children with PH admitted to the PICU represent a high-risk group, with a mortality rate significantly greater than that of the general PICU population (2). Our group previously identified age less than 6 months or greater than 16 years, invasive mechanical ventilation, and co-diagnoses of heart failure, sepsis, hemoptysis, disseminated intravascular coagulation, stroke, and multi-organ dysfunction syndrome as factors associated with mortality for children with PH in the PICU (2). Similarly, in the general inpatient pediatric PH population, sepsis, respiratory failure, acute renal failure, hepatic insufficiency, arrhythmias, and the use of ECMO have been associated with mortality (29). Other factors associated with worse outcomes for children with PH identified to date include higher baseline pulmonary vascular resistance index, higher B-type natriuretic peptide levels, higher mean right atrial pressure, lower cardiac index (30–38), higher (worse) World Health Organization Functional Class (32, 33, 37) and higher Pediatric Functional Class (25, 39).

While prior studies have identified individual factors associated with greater mortality, PIPHM is the first attempt to incorporate demographic, clinical, and procedural variables available within the first 12 hours of admission to the PICU to predict mortality in children with PH. The final tool incorporates 14 factors in a single prognostic model: age, bradycardia, systolic hypotension, tachypnea, pH, FiO₂, hemoglobin, BUN, creatinine, mechanical ventilation, non-elective admission, previous PICU admission, PICU admission due to non-surgical cardiovascular disease, and cardiac arrest immediately prior to admission. The majority of these factors are included in either the PRISM-3 or PIM-2 scores, which are standardly used for assessment of illness severity upon admission to the PICU. However, given that these tools were developed from heterogeneous patient samples, it is not surprising that in children with PH the PIPHM model performs superiorly to PRISM-3 and PIM-2. Additionally, the PIPHM model is more parsimonious to PRISM-3, with 14 compared to 25 variables. This improved performance may reflect the inclusion of factors not present in PRISM-3 or PIM-2, such as age and bradycardia, or due to the

exclusion of factors present in these other models, including those related to neurologic status and infection, which may be less relevant to the PH population.

As expected, variables concerning for impaired oxygen delivery, such as anemia and increased FiO₂, and compromised hemodynamics, such as acidosis, bradycardia and low systolic blood pressure, are associated with higher risk of mortality in this patient population (24). Similarly, the presence of high BUN and high creatinine, which often reflect low cardiac output or shock, suggest that renal function is an important prognostic indicator in these patients. This is consistent with other studies of pediatric PH patients in the inpatient setting, which identified acute renal failure (29) and need for renal support (2) as predictors of mortality. Consistent with our prior study, which found invasive mechanical ventilation to be significantly associated with mortality (2), tachypnea and need for mechanical ventilation were included in the final model. Non-elective PICU admission, prior PICU admission, and cardiac arrest prior to admission likely identify those patients with more severe underlying disease and therefore lower likelihood of survival.

Overall, PIPHM appears to be more suitable for predicting PICU mortality among children with PH than other existing pediatric critical care illness severity scores. PIPHM, like PIM-2 and PRISM-3, could be incorporated as part of a standardized assessment of likelihood of mortality in clinical research studies. Additionally, clinicians could incorporate an understanding of the components comprised in PIPHM in their assessment of disease severity and in discussions with families in the PICU regarding prognosis. For example, earlier identification of patients at higher risk for mortality may facilitate escalation of therapy, such as initiation of ECMO or renal replacement therapy. The logistic prediction model developed in this study could easily be incorporated into an online calculator. However, before this tool is used in the clinical setting, a prospective validation of the PIPHM model is indicated in future studies to better understand how evaluation and targeted management of components of the PIPHM score will actually influence outcome.

This study has several important limitations. The data were collected retrospectively and relied on accurate database entry based on chart review, including for the accurate identification and classification of PH diagnoses as no echocardiography, hemodynamic, or pharmacologic data were available for confirmation. Timing, duration, and etiology of PH diagnosis were not captured in this database. Moreover, the role of congenital heart disease was not assessed in this model and warrants future investigation. Additionally, PIPHM only includes variables present within the first 12 hours of admission. Predictors of mortality identified in our group's initial study from this same database (2), including comorbidities and procedures other than mechanical ventilation, were not considered candidate variables for the PIPHM. Therefore, this model does not capture the effect of comorbidities and procedures performed throughout admission, many of which were associated with mortality (2). The development of the model relied on several assumptions and manipulations of variables that may limit its accuracy. All missing values for variables included in PRISM-3 and PIM-2 were assumed to be in the normal range. This assumption is more sound for those variables included in PRISM-3, where clinicians have a 12-hour period to obtain labs, as compared to PIM-2, which only gives a 1-hour window to obtain laboratory values. While great effort was made to determine appropriate thresholds for vital sign ranges by age

category based upon consensus guidelines, little external evidence was available to inform the choice of thresholds for other variables, such as hemoglobin, BUN, creatinine, FiO₂. Therefore, we relied on interpretation of descriptive statistics and collective clinical judgment. Overall, the limitations are mitigated by the large, multicenter patient sample and superior performance of the model in both training and validation cohorts. Validation in other large datasets would provide further support for the model.

Conclusion

The PIPHM is a parsimonious model that performs better than the PRISM-3 and PIM-2 scores for mortality in a multicenter cohort of pediatric PH patients admitted to PICUs. Although additional validation might be warranted, this PH-specific score could facilitate early identification of patients at high risk for mortality, with more rapid initiation of appropriate treatment, improve counseling and prognostication for patients and families, and be useful as a clinical research tool.

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Abbreviations

AUC	area under the curve
BUN	blood urea nitrogen
CI	confidence interval
ECMO	extra-corporeal membrane oxygenation
ICD9	International Classification of Diseases, Ninth Revision
PaO₂	arterial partial pressure of oxygen
PaCO₂	arterial partial pressure of carbon dioxide
mPAP	mean pulmonary artery pressure
OR	odds ratio
PICU	pediatric intensive care unit
PIM-2	Pediatric Index of Mortality-2
PIPHM	Pediatric Index of Pulmonary Hypertension Intensive Care Mortality

PH	pulmonary hypertension
PPHN	persistent pulmonary hypertension of the newborn
PRISM-3	Pediatric Risk of Mortality-3
ROC	Receiver operating characteristic
VPS	Virtual Pediatric Systems

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Figure 1.

Receiver operating characteristic (ROC) curve for Pediatric Index of Pulmonary Hypertension Intensive Care Mortality (PIPHM) versus Pediatric Index of Mortality (PIM)-2 and Pediatric Risk Mortality (PRISM)-3 using the training dataset (n = 10,472).

Figure 2.

Receiver operating characteristic (ROC) curve for Pediatric Index of Pulmonary Hypertension Intensive Care Mortality (PIPHM) versus Pediatric Index of Mortality (PIM)-2 and Pediatric Risk Mortality (PRISM)-3 using the validation dataset (n = 3,490).

Table 1

Candidate Variables for Prognostic Model

Candidate Variable	Relevance
<i>Demographic</i>	
Age	Demographic
Gender	Demographic
<i>Clinical</i>	
History of prematurity	Diagnostic
PH group	Diagnostic
FiO ₂	PIM2
Mechanical ventilation within 12 hours of admission	PIM2, PRISM3
<i>Vital signs</i>	
Systolic blood pressure	PRISM3, PIM2
Heart rate	PRISM3
Respiratory rate	PRISM3
<i>Laboratory analyses</i>	
pH	PIM2
Base excess	PIM2
PaO ₂	PRISM3, PIM2
PaCO ₂	PRISM3
Hemoglobin	PRISM3
Blood urea nitrogen	PRISM3
Creatinine	PRISM3
<i>Other factors</i>	
Non-elective admission (includes admission from inpatient)	PRISM3, PIM2
Previous PICU admission	PRISM3
Acute problem requiring PICU admission associated with a medical (or non-surgical) cardiovascular disease	PRISM3
Cardiac arrest immediately prior to admission	PRISM3, PIM2
Patient admitted following cardiac surgery or procedure	PRISM3, PIM2

Abbreviations: PH – pulmonary hypertension; FiO₂ – fraction of inspired oxygen; PaO₂ – arterial partial pressure of oxygen; PaCO₂ – arterial partial pressure of carbon dioxide; PICU – pediatric intensive care unit; PIM2 – Pediatric Index of Mortality-2; PRISM-3 - Pediatric Risk of Mortality-3.

Table 2

Candidate Variables as Univariate Predictors of Mortality

Characteristic ^d	n	Mortality n (%)	Crude OR
Demographic			
Age			
0 to 6 months	3,501	383 (10.9)	3.1 (2.4-3.8)
>6 to 12 months	2,463	154 (6.3)	1.7 (1.3-2.2)
>12 months to 2 years	2,521	109 (4.3)	1.1 (0.9-1.5)
>2 to 5 years	2,639	102 (3.9)	Reference
>5 to 16 years	2,453	157 (6.4)	1.7 (1.3-2.2)
>16 years	691	66 (9.6)	2.6 (1.9-3.7)
Gender, male	7,010	505 (6.7)	1.0 (0.9-1.1)
Clinical			
History of prematurity	2,311	165 (6.7)	1.0 (0.8-1.2)
PH group			
Primary PH	1,885	173 (8.4)	Reference
Secondary PH	11,412	798 (6.5)	0.8 (0.6-0.9)
FiO ₂ > 60% ^b	1,471	209 (14.2)	2.6 (2.2-3.1)
Mechanical ventilation	7,713	788 (9.3)	3.1 (2.6-3.7)
Vital signs (within 12 hours of admission)			
Systolic hypotension for age ^c	5,777	605 (10.5)	2.6 (2.2-3.0)
Heart rate for age			
Normal	8,415	489 (5.8)	Reference
Tachycardia ^d	4,956	401 (8.1)	1.4 (1.2-1.6)
Bradycardia ^e	897	81 (9.0)	1.6 (1.3-2.1)
Tachypnea for age ^f	1,921	182 (9.5)	1.5 (1.3-1.8)
Laboratory analyses (within 12 hours of admission)			
pH 7.3 ^g	2,813	420 (14.9)	3.5 (3.0-4.0)
Base deficit < -4 ^h	767	140 (18.3)	3.4 (2.8-4.1)
PaO ₂ < 100 ⁱ	3,013	396 (13.1)	2.8 (2.5-3.2)
PaCO ₂ > 55 ^j	2,997	378 (12.6)	2.6 (2.3-3.0)
Hemoglobin (mg/dL) ^k			
<6	72	17 (23.6)	4.7 (2.7-8.2)
6-15	13,072	806 (6.2)	Reference
>15	1,124	148 (13.2)	2.3 (1.9-2.8)
Blood urea nitrogen > 20 (mg/dL) ^l	1,767	259 (14.7)	2.8 (2.4-3.3)
Creatinine > 0.6 (mg/dL) ^m	1,948	299 (15.4)	3.1 (2.7-3.7)
Other factors			
Non-elective admission ⁿ	10,315	864 (8.4)	3.3 (2.7-4.0)

Characteristic ^a	n	Mortality n (%)	Crude OR
Previous PICU admission ⁿ	2,910	357 (12.3)	2.4 (2.1-2.8)
PICU admission for non-surgical heart disease ⁿ	4,041	349 (8.6)	1.6 (1.4-1.7)
Admission after cardiac surgery or procedure	2,991	220 (7.4)	1.1 (0.9-1.3)
Cardiac arrest immediately prior to admission ^o	341	98 (28.7)	6.0 (4.7-7.7)

Abbreviations: PH – pulmonary hypertension; FiO₂ – fraction of inspired oxygen; PaO₂ – arterial partial pressure of oxygen; PaCO₂ – arterial partial pressure of carbon dioxide; PICU – pediatric intensive care unit.

^a n=14,268 unless otherwise specified.

^b Chosen based upon median = 0.65 (n = 2,343)

^c Systolic hypotension defined as 70+(age × 2): Age < 2 years: SBP<70; Age 2-5 years: SBP<80; Age 6-12 years: SBP<90; Age 13 years: SBP<100. n = 13,930.

^d Tachycardia defined as: Age < 2 years: HR>180; Age 2-5 years: HR>140; Age 6-12 years: HR>130; Age 13 years: HR>110. n =13,946.

^e Bradycardia defined as: Age <2 years: HR<90; Age 2-5 years: HR<60; Age 6-12 years: HR<60; Age 13 years: HR<50. n =13,946.

^f Tachypnea defined as 2.5 times the upper limit of normal for age: Age < 2 years: RR>85; Age 2-5 years: RR>55; Age 6-12 years: RR>45; Age 13 years: RR>35. n=13,851.

^g Based upon median pH = 7.31, mean pH = 7.29. n=6,146.

^h Based upon 25th percentile (median -0.9, mean -0.3). n=3,441.

ⁱ Based upon median 91, mean 132. Does not take into account FiO₂ because we do not know if data are from the same points in time. n=3,894.

^j Based on median 52, mean 55. n=7,458.

^k Based upon Pediatric Cardiac Intensive Care paper in PCCM. n=7,743.

^l Based upon clinical relevance, 75th percentile = 19. n=7,948.

^m Based upon clinical relevance, 75th percentile = 0.6. Not adjusted for age. n=7,949.

ⁿ Includes all admissions to the ICU from other inpatient units (missing in 308 cases).

^o Missing in 308 cases.

Table 3

Variables Included in Pediatric Index of Pulmonary Hypertension Intensive Care Mortality (PIPHM)

Variable	Type
Age	Categorical
FiO ₂	Dichotomous
Mechanical ventilation	Dichotomous
Systolic hypotension	Categorical, age-adjusted
Bradycardia	Categorical, age-adjusted
Tachypnea	Categorical, age-adjusted
pH	Dichotomous
Hemoglobin	Categorical
Blood urea nitrogen	Dichotomous
Creatinine	Dichotomous
Non-elective admission	Dichotomous
Previous PICU admission	Dichotomous
PICU admission for non-surgical heart disease	Dichotomous
Cardiac arrest immediately prior to admission	Dichotomous

Abbreviations: FiO₂ – fraction of inspired oxygen; PICU – pediatric intensive care unit.

Table 4**Multivariate Predictors of Mortality**

Characteristic	n	Mortality n (%)	Crude OR	Adjusted OR
Age				
0 to 6 months	2,594	310 (12.0)	3.3 (2.5-4.3)	1.9 (1.4-2.5)
>6 to 12 months	1,798	111 (6.2)	1.6 (1.2-2.1)	1.4 (1.0-1.9)
>12 months to 2 years	1,825	78 (4.3)	1.1 (0.8-1.5)	1.0 (0.7-1.4)
>2 to 5 years	1936	77 (3.9)	Reference	Reference
>5 to 16 years	1808	110 (6.1)	1.6 (1.7-3.6)	1.2 (1.0-2.3)
>16 years	510	47 (9.2)	2.5 (1.7-3.6)	1.5 (1.0-2.3)
FiO ₂ > 60%	1,105	164 (14.8)	2.7 (2.2-3.2)	1.5 (1.2-1.9)
Mechanical ventilation	6,321	599 (9.5)	3.1 (2.6-3.8)	2.1 (1.7-2.6)
Systolic hypotension for age	4,301	468 (10.9)	2.7 (2.3-3.2)	1.6 (1.3-1.9)
Bradycardia for age	679	63 (9.3)	1.4 (1.1-1.8)	1.6 (1.2-2.1)
Tachypnea for age	1,669	185 (11.1)	1.9 (1.6-2.4)	1.8 (1.5-2.1)
pH 7.3	2,103	324 (15.4)	3.5 (3.0-4.1)	1.7 (1.4-2.1)
Hemoglobin (mg/dL)				
<6	54	14 (25.9)	5.2 (2.8-9.6)	2.5 (1.1-5.7)
6-15	9,559	605 (6.3)	Reference	Reference
>15	858	114 (13.3)	2.3 (1.8-2.8)	1.2 (0.9-1.5)
Blood urea nitrogen > 20 (mg/dL)	1,316	191 (14.5)	2.7 (2.3-3.2)	1.6 (1.3-2.0)
Creatinine > 0.6 (mg/dL)	1,467	237 (16.2)	3.3 (2.8-3.9)	1.4 (1.1-1.8)
Non-elective admission	7,563	645 (8.5)	3.0 (2.4-3.8)	2.9 (2.3-3.7)
Previous PICU admission	2,194	281 (12.8)	2.5 (2.2-3.0)	1.9 (1.6-2.3)
PICU admission for non-surgical heart disease	2,996	268 (8.9)	1.5 (1.3-1.7)	1.4 (1.2-1.7)
Cardiac arrest immediately prior to admission	257	70 (27.2)	5.4 (4.1-7.2)	2.6 (1.9-3.5)

This table includes admissions from training dataset cohort only (n = 10,472). Values reported are from within first 12 hours of admission.

Abbreviations: FiO₂ – fraction of inspired oxygen; PICU – pediatric intensive care unit; OR – odds ratio.